REMARKS

Claim 13, as amended, and claims 14-17 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejection of claims 13-17 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 13-17 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. The Action states that it is unclear whether the negative proviso "but not the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6)" in claim 13 is to be applied to a. and b. in addition to c., or is exclusive to c.

Applicants contend that one of ordinary skill in the art would understand that the portion of claim 13 beginning with "P^1, P^2, P^3, and P^4 are each independently" and ending with the proviso "but not the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6)" means that any one of P^1, P^2, P^3, and P^4 can be the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), or the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13), and that any one of P^1, P^2, P^3, and P^4 cannot be the extracellular region of TACI (SEQ ID NO: 15) or the extracellular region of BCMA (SEQ ID NO: 6). Applicants, therefore, contend that claim is not indefinite. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 13 to replace the designations "a," "b," and "c" with the designations "i," "ii," and "iii," and to indent both parts i, ii, and iii, as well as the negative proviso. Applicants contend that the newly indented portions of claim 13 serve to limit the parts of the claimed composition of matter designated P^1, P^2, P^3, and P^4. Applicants, therefore, respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

2. Rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph

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The Office Action asserts a rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that claims 13-15 do not limit the functional attributes of the encompassed molecules, and that one of ordinary skill in the art would reasonably conclude that claims 13-15 are not limited to binding AGP-3 or APRIL. The Action also states that the disclosure of TACI and BCMA as receptors for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor, does not adequately describe the claimed genus because the molecules of the claimed genus need only minimally comprise the consensus regions of the extracellular domains of TACI and BCMA, and therefore, differ significantly in structure from the extracellular portions of TACI and BCMA. The Action also states that the disclosure of TACI and BCMA as receptors for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor, does not adequately describe the claimed genus because the claimed genus encompasses molecules that do not bind to AGP-3 or APRIL, and therefore, the molecules of the claimed genus differ significantly in function from the extracellular portions of TACI and BCMA.

Applicants respectfully disagree with the Action's assertion that the specification does not contain an adequate written description of the claimed invention. Applicants note that the *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement* ("*Guidelines*") state that an adequate written description of the claimed invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Guidelines,* 66 Fed. Reg. 1099, 1105 (2001). With regard to a claim directed to a genus, the *Guidelines* specifically state that the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, *or* reduction to drawings, *or* by disclosure of relevant, identifying characteristics (*i.e.*, structure *or* other physical *or* chemical properties, *or* by functional characteristics coupled with a known or disclosed correlation between function and structure, *or* by a combination of such identifying characteristics) sufficient to show the applicant was in possession of the claimed genus. *Guidelines,* 66 Fed. Reg.

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1099, 1106 (2001) (*emphasis added*).

The specification explicitly teaches that (a) TACI and BCMA are cell-surface receptors for APRIL (page 60, lines 14-19); (b) APRIL competes with AGP-3 for TACI and BMCA binding (page 60, lines 15-18); (c) soluble BMCA competes with APRIL and AGP-3 for receptor binding, ameliorating T cell-dependent and T cell-independent humoral immune responses *in vivo* (page 5, lines 7-10; page 60, lines 25-27); and (d) soluble TACI competes with APRIL and AGP-3 for receptor binding, ameliorating T cell-dependent and T cell-independent humoral immune responses *in vivo* (page 5, lines 10-12; page 60, lines 24-27). The specification also explicitly teaches molecules such as those recited in claims 13-16, comprising at least one specific binding partner, wherein a "specific binding partner" is a molecule that preferentially binds to a protein of interest (*e.g.*, TACI and BCMA), including molecules such as solublized receptors (*e.g.*, soluble TACI and soluble BCMA) (page 13, lines 14-19; page 32, line 22 to page 33, line 18). The specification also explicitly teaches that soluble receptor fragments such as the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), and the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13) constitute specific binding partners (page 33, line 24 to page 34, line 3). Thus, the specification's teachings clearly show that disease states associated with APRIL and AGP-3 activity can be modulated using TACI, BCMA, APRIL, or AGP-3, or portions thereof, either individually or in combination (page 5, lines 19-27).

Applicants contend that because the specification explicitly discloses relevant, identifying characteristics of the molecules encompassed by claimed genus, and because the claims are limited to molecules comprising at least one of three soluble receptor fragments explicitly disclosed in the specification (*i.e.*, the consensus region of TACI, the consensus region of BCMA, and the TACI/BCMA extracellular consensus sequence), the specification contains an adequate written description of the claimed invention. Applicants, therefore, respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

3. Rejections of claims 13-15 under 35 U.S.C. § 103(a)

The Office Action asserts a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 98/39361 (the '361 publication), in view of

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International Publication No. WO 99/11791 (the '791 publication). The Action states that the '361 publication discloses (a) chimeric TACI proteins comprising the extracellular domain of TACI linked to the Fc domain of an immunoglobulin, a glycosylphospholipid, a natural protein such as a transferrin or hormone, or a synthetic protein; (b) that TACI comprises two cysteine-rich repeats at residues 33-66 and 70-104 which indicate that TACI is a member of the TNF receptor superfamily; and (c) a blocking reagent comprising a recombinant form of the extracellular portion of TACI that acts to intercept the normal endogenous ligands which bind to and activate TACI. The Action also states that the '361 publication does not disclose a composition comprising a portion of the TACI extracellular domain, wherein the composition comprises the TACI consensus sequence but not the entirety of the TACI extracellular domain. The Action also states that the '791 publication discloses that cysteine-rich pseudo-repeats in the extracellular domain of the TNF receptor family are involved in ligand binding. The Action concludes that it would have been *prima facie* obvious at the time the claimed invention was made to substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins disclosed in the '361 publication, and that one of ordinary skill in the art would be motivated to do so by the disclosure in the '361 publication that a recombinant form of the extracellular portion of TACI acts to intercept the normal endogenous ligands which bind TACI and the disclosure in the '791 publication that cysteine repeat regions of members of the TNF receptor family are important for ligand binding.

Applicants note that an analysis of obviousness must be based on the following factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviosuness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Moreover, where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 *also requires* consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). As the Federal Circuit has emphasized: "[b]oth the suggestion and the reasonable expectation of success must be

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founded in the prior art, not the Applicants' disclosure." *Id.*

Applicants respectfully disagree with the Action's assertion that the '361 and '791 publications, when taken together, render the claimed invention obvious. In particular, Applicants contend that this combination of references does not suggest that one of ordinary skill in the art should make the claimed composition. For example, while the '791 publication discloses that cysteine-rich pseudo-repeats in the extracellular domains of TNF receptor superfamily members are *involved* in ligand binding (page 7, lines 24-29), on several occasions this reference also refers to the *entire* extracellular domain as a ligand-binding domain (*see, e.g.*, page 9, lines 15-17). Moreover, in noting that members of the TNF receptor superfamily share between 16-60% sequence identity in their extracellular ligand-binding domains (page 9, lines 15-19), and that the extracellular domains of these members vary greatly in size (Figures 1A-1B), the '791 publication acknowledges the substantial sequence diversity that exists among the members of this superfamily. Thus, the '361 and '791 publications, when taken together, do not suggest that one of ordinary skill in the art substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins disclosed in the '361 publication, because one of ordinary skill in the art, without considering Applicants' disclosure, would *not* have a reasonable expectation of success in making a composition comprising at least one of the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), or the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13) that could modulate TACI, BCMA, APRIL, or AGP-3 activity. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over U.S. Patent No. 6,475,987 (the '987 patent), in view of International Publication No. WO 99/11791 (the '791 publication). The Action states that the '987 patent discloses (a) that BCMA is a member of the TNF receptor family and that BCMA is the receptor for TALL-1; (b) that fusion proteins comprising one or more extracellular domains of BCMA can be used in a non-cell based screening assay to identify compounds that bind BCMA; and (c) a composition comprising the extracellular domain of BCMA fused to the Fc domain of an immunoglobulin. The Action also states that the '791 publication discloses that cysteine-rich pseudo-repeats in the extracellular domain of the TNF receptor family are involved in ligand binding. The Action concludes that it would have

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been *prima facie* obvious at the time the claimed invention was made to substitute a polypeptide comprising the cysteine-rich repeat of the BCMA extracellular domain in the fusion protein comprising the immunoglobulin Fc domain disclosed in the '987 patent, and that one of ordinary skill in the art would be motivated to do so by the disclosure in the '791 publication that cysteine repeat regions of members of the TNF receptor family are important for ligand binding.

Applicants respectfully disagree with the Action's assertion that the '987 patent and the '791 publication, when taken together, render the claimed invention obvious. In particular, Applicants contend that this combination of references does not suggest that one of ordinary skill in the art should make the claimed composition. As described above, while the '791 publication discloses that cysteine-rich pseudo-repeats in the extracellular domains of TNF receptor superfamily members are *involved* in ligand binding (page 7, lines 24-29), on several occasions this reference also refers to the *entire* extracellular domain as a ligand-binding domain (*see, e.g.*, page 9, lines 15-17). Moreover, in noting that members of the TNF receptor superfamily share between 16-60% sequence identity in their extracellular ligand-binding domains (page 9, lines 15-19), and that the extracellular domains of these members vary greatly in size (Figures 1A-1B), the '791 publication acknowledges the substantial sequence diversity that exists among the members of this superfamily. Thus, the '987 patent and the '791 publication, when taken together, do not suggest that one of ordinary skill in the art substitute a polypeptide comprising the cysteine-rich repeat of the BCMA extracellular domain in the fusion protein comprising the immunoglobulin Fc domain disclosed in the '987 patent, because one of ordinary skill in the art, without considering Applicants' disclosure, would *not* have a reasonable expectation of success in making a composition comprising at least one of the consensus region of TACI (SEQ ID NO: 16), the consensus region of BCMA (SEQ ID NO: 7), or the TACI/BCMA extracellular consensus sequence (SEQ ID NO: 13) that could modulate TACI, BCMA, APRIL, or AGP-3 activity. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 103(a) have been traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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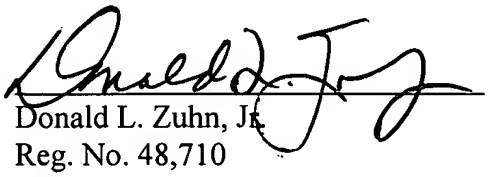
CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Canella believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: June 1, 2005

By: 
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